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ANTI-OBESITY EFFECT OF GUDUCHI TRIPHALA KWATHA WITH SHILAJATHU AS A PRAKSHEPA CHURNA

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ABSTRACT

Obesity is one of the most common public health problems in both developed and developing countries. Obesity is defined as body fat content of more than 20 % in average adult males and over 30 % in females. In this study the efficacy of *Guduchi Triphala Kwatha* added with *Shilajathu* as *Prakshepa Churna* in High Fat Diet induced obese Wistar rats were evaluated. Significant result was obtained in anti-obesity parameters after treatment.

KEYWORDS: Obesity, *Sthoulya, Guduchi Triphala Kwatha, Shilajathu.*

INTRODUCTION

Obesity is a chronic multifactorial medical condition characterized by excess body fat that devolops as result of long-term energy imbalance, which means the excessive caloric consumption and insufficient energy output. This extra energy gets accumulated in the form of adipose tissue.[1] In *Ayurveda,* Obesity can be compared to *Sthoulya*. *Acharya Charaka* in *Sutrasthana* states, *Athisthoola* person with excessive accumulation of *Medas* and *Mamsa* leading to flabbiness of hips, abdomen and breast. *Athisthoola* has been categorized as one of the *Ashta Nindithiya Purusha* and is at risk of developing various complications.[2] *Guduchi Triphala Kwatha* added with *Shilajathu* mentioned in *Vangasena Samhitha* in *Sthoulya chikitsa* is selected for the study.[3] *Guduchi* is *Kapha Vatagna, Rasayana, Pittamedovishoshana.*[4] *Triphala* is *Rasayanavara, Kledamedohara.*[5] *Shilajathu* is *Medachedokara* and *Rasayana.*[6]

METHODOLOGY

The study was designed as 3 Groups – Control group, Standard group and Trial group, 6 rats were assigned in each groups. Obesity was induced with High Fat Diet (HFD) in the Wistar rats weighing 200 – 225g. When the rats attain 325 - 350g, considered as obese,[7] and selected for the study. High Fat Diet was made with standard pellet added with Vanaspathi Dalda and coconut oil in the ratio of 3: 2.[8,9,10] It was continued in all the groups throughout the study. Group 1 was the Control group administered with distilled water (9.86ml/kg). Group 2 received Standard drug Orlistat (30mg/kg).[11] Group 3 was given with *Kwatha* (9.86 ml/kg)[12] added with *Shilajathu* (308.33 mg/kg).[12] All the drugs were administered orally once a day for a period of 30 days. Body weight, food and water consumption were recorded daily.[13] The BMI was calculated using the formula, BMI =Body Weight (g)/Length (cm2). Body length (nose-to-anus length) of the experimental animals were measured on 1st and 30th day of the study period. Waist circumference will also be measured on the 1st and 30th day of the study period on the largest zone of the rat abdomen using a plastic non extensible measuring tape by keeping the rats in ventral position.[13] Biochemical parameters such as Glucose, Insulin, Total cholestrol, Leptin, Lipid Peroxides (LPO), Glutathione (GSH), Superoxide Dismutase (SOD), Catalase were assessed on 1st and 30th day of the study period. Histopathological analysis of liver, kidney and adipose tissue were done by sacrificing the rats after 24 h observation period of the last dose of administration of the drug.[14,15]

RESULTS

1. DATA RELATED TO INDUCTION OF OBESITY Alamgeer, Aqsa G, Taseer A, Muhammad NM. Antihyperlipidemic effect of Berberis orthobotrys in hyperlipidemic animal models. Bangladesh J Pharmacol, 2014; 9: 377-382.

Munshi RP, Joshi SG, Rane BN. Development of an experimental diet model in rats to study hyperlipidemia and insulin resistance, markers for coronary heart disease. Indian J Pharmacol, 2014 May-Jun; 46(3): 270-6.

Jeevangi Santoshkumar1, Manjunath S2, Sakhare Pranavkumar M. A study of anti-hyperlipidemia, hypolipedimic and anti-atherogenic activity of fruit of *Emblica officinalis* (amla) in high fat fed albino rats. Int J Med Res Health Sci. 2013; 2(1): 70-77.

For the induction of obesity HFD was given to each group and weekly assessment of body weight was done. There was 50% increase in body weight in all the groups. The results of mean body weight of rats were shown in table 4.

Table 1: Increase in body weight during induction of obesity. Time period - 6 weeks.

Groups		Initial	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6
Control	Mean ± SD	215 ±10	231.7 ± 16	255.8± 14.6	284.2 ± 16.8	298.3 ± 15	312.5 ± 19.2	324.2± 21
	SEM (±)	4.08	6.54	5.97	6.88	6.15	7.83	8.6
	%change in body weight	0	7.75	10.43	11.07	4.99	4.75	3.73
Standard	Mean ± SD	211.7 ± 8.2	224.2 ±7.4	252.5 ± 6.12	278.3 ± 10.8	293.3 ± 12.5	307.5 ± 11.7	318.3 ± 11.6
	SEM (±)	3.33	3	2.5	4.41	5.11	4.79	4.77
	%change in body weight	0	5.91	12.64	10.23	5.39	4.83	3.52
Trial	Mean ± SD	205.8 ± 4.9	220 ± 7.7	242.5 ± 12.5	256.6 ± 19.4	280 ± 17.3	293.3± 16.3	303.3 ± 12.1
	SEM (±)	2.01	3.16	5.12	7.92	7.07	6.67	4.94
	%change in body weight	0	6.88	10.23	5.84	9.09	4.76	3.41

2. DATA RELATED TO RESPONSE TO TREATMENT

Data related to food intake of animals and body weight were taken daily for a period of 30 days of treatment after induction of obesity. Other measurements (BMI, WC, Biochemical parameters) before and after treatment were collected from each group and statistically analyzed using One-way ANOVA test. Values are expressed as Mean, Standard Error of Mean, Standard Deviation and Percentage of Change. All charts and graphs are present with Title "MEAN". The difference between each group were considered statistically significant at $P < 0.05$. The details of analysis is given in the following sections.

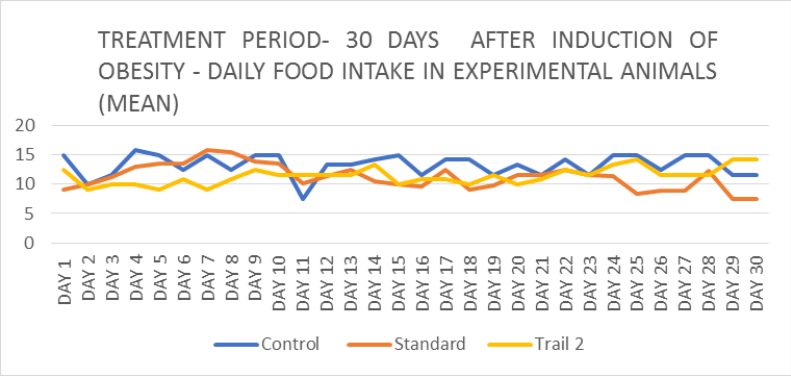


Figure 1: Data related to daily food intake.

The daily food intake of experimental rats was measured and the obtained results were presented in form of average food intake. The percentage increase in daily food intake of the Control group is 22%. The percentage decrease in daily food intake of Standard was 41% and that of Trial group was 14%.

Table 2: Effect of treatment on body weight.

	Control	Standard	Trial
1	380	310	265
2	350	320	283
3	390	300	271
4	342	300	282
5	342	280	295
6	370	300	282
Mean	362.33	301.67	279.67
SEM± SD	8.39±20.56	300.27±5.17	4.27±10.46
%Change	11.77	-5.23	-7.8

Statistically significant result was obtained in bodyweight of trial group when compared to control and standard group.

Table 3: Effect of treatment on Body Mass Index (g/cm^2).

Groups	BT			AT	
	Mean± SD	SEM	Mean ± SD	SEM	% Change
Control	0.79 ±0.04	0.02	0.82 ± 0.04	0.02	3.59
Standard	0.82 ± 0.1	0.04	0.73 ± 0.07	0.03	-11.16
Trial	0.85 ± 0.1	0.04	0.72 ± 0.05	0.02	-14.96

Statistically significant result was obtained in BMI of trial group when compared to control and standard group.

Table 4: Effect on Waist circumference (cm).

Groups	BT			AT		
	Mean± SD	SEM	% Change	Mean ± SD	SEM	% Change
Control	18.17± 1.4	0.57	0	18.8 ± 1.37	0.56	3.67
Standard	17.33±1.47	0.6	0	18.9 ± 1.48	0.61	9.04
Trial	19.48±2.09	0.85	0	17.57±1.21	0.49	-9.84

Waist circumference of all groups were within normal limits before and after treatment when compared to normal reference rats.

Table 5: Effect on blood insulin level (pg/ml).

Groups	BT			AT		
	Mean± SD	SEM	% Change	Mean ± SD	SEM	% Change
Control	125.75±39.9	16.28	0	112.17±55.7	22.77	-10.8
Standard	130.65±30.5	12.45	0	121.53±33.5	13.69	-6.98
Trial	103.85±68.7	28.05	0	73.09±14.08	5.75	-29.62

Statistically significant result was obtained in blood insulin levels of trial group when compared to control and standard group but not within normal limits.

Table 6: Effect on Total Cholestrol TC (mg/dl).

		TC (mg/dl)	
		BT	AT
Control	Mean ± SD	145.8± 16.7	146.1± 14.4
	SEM (±)	6.84	5.88
Standard	Mean ± SD	136.0± 6.01	106.1± 4.8
	SEM (±)	2.45	1.94
Trial	Mean ± SD	171.0± 19.3	143.2± 8.3
	SEM (±)	7.89	3.4

Statistically insignificant result was obtained in total cholestrol levels of trial group when compared to control and standard group but there was considerable mean difference after treatment.

Table 7: Effect of treatment on Antioxidant markers.

		LPO		ANTIOXIDANTS					
		MDA (nmols/mg protein)		GSH (nmols/ mg protein)		SOD (U/mg protein)		CAT (U/mg protein)	
		BT	AT	BT	AT	BT	AT	BT	AT
Control	Mean	14.41±1.9	14.79±1.8	6.37± 0.2	6.1± 0.03	0.09±0.02	0.1±0.02	3.65±1.23	2.93±3.51
	SEM(±)	0.79	0.71	0.08	0.01	0.01	0.01	0.5	1.43
Standard	Mean	14.5± 0.55	2.03± 0.8	9.5±2.03	13.09± 4.9	0.09± 0	0.18± 0.04	5.5± 4.5	2.55± 0.5
	SEM(±)	0.22	0.33	0.83	1.99	0	0.02	1.85	0.2
Trial	Mean	8.05± 0.05	5.27± 1.2	5.6± 1.03	13.05± 8.8	0.1± 0.02	0.12± 0.04	2.3 ± 0.9	2.83± 0.7
	SEM(±)	0.02	0.49	0.42	3.58	0.01	0.02	0.35	0.3

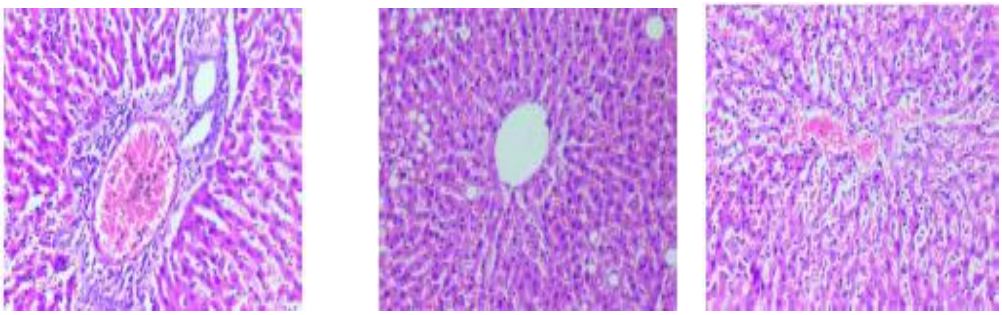
Statistically significant result was obtained in lipid peroxidation levels and antioxidant enzyme activity levels of trial group when compared to control and standard group.

Table 8: Effect on blood leptin levels (pg/ml).

BLOOD LEPTIN LEVELS (pg/ml)			
		BT	**AT**
Control	**Mean**	1318.5± 9.79	1249.07±81.68
	SEM (±)	4	33.34
Standard	**Mean**	391.24±1.21	333.78±1.22
	SEM (±)	0.5	0.5
Trial	**Mean**	445.95±128.43	281.95±12.13
	SEM (±)	52.43	4.95

Statistically significant result was obtained in blood leptin levels of trial group when compared to control and standard group.

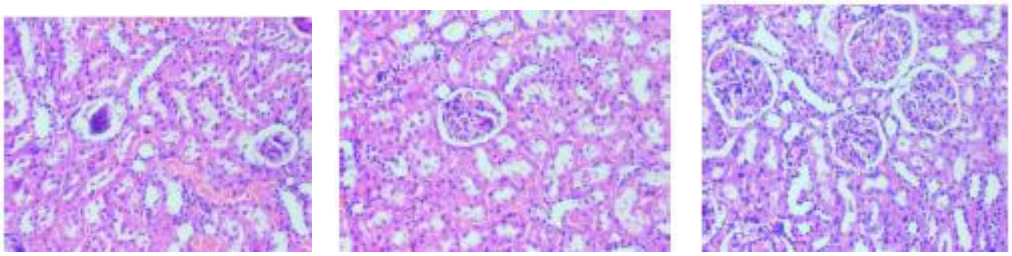
HISTOPATHOLOGICAL EVALUATION OF ORGANS



Control group **Standard group** **Trial group**

Figure 2: Liver.

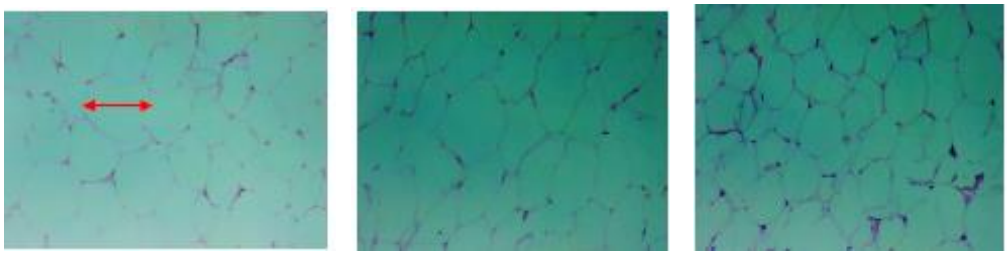
Control: Central venous congestion, severe sinusoidal dilatation and congestion, hepatocyte degeneration and Kupffer cell hyperplasia; Standard: Mild hepatocyte degeneration with mild sinusoidal dilatation and congestion, mild periportal edema: Trial: Central and portal venous congestion, severe to mild sinusoidal dilatation and congestion, mild hepatocyte degeneration, mononuclear cell infiltration and Kupffer cell hyperplasia were noted while analysing the histopathology slides.



Control group **Standard group** **Trial group**

Figure 3: Kidney.

Control: Glomerular atrophy, renal tubular degeneration and intertubular hemorrhage, widened Bowman's space. Standard: Mild renal tubular degeneration and intertubular hemorrhage, widened Bowman's space; Trial: Mild to moderate renal tubular degeneration, intertubular hemorrhage and hyperaemic glomerular tuft with vacuolation. Moreover, widened Bowman's spaces were also noted on histopathology slides.



Control group **Standard group** **Trial group**

Figure 4: Adipose Tissue.

Control: Increased size of adipocytes; Standard: Increased size of adipocyte: Trial: Adipocytes with normal and increased size but majority having big size.

DISCUSSION

Obesity is characterised by increased adipose tissue mass which can trigger a cascade of metabolic disturbances, insulin resistance, and proinflammatory responses. So addressing obesity is a pressing concern globally, making it a relevant and impactful area of research. A gain in body weight is a common index of obesity. In this study, HFD was fed for 6 weeks and there was 50% weight gain in all groups.

Effect on daily food intake and Leptin levels: Daily food intake of the Control group was increased after treatment while it decreased in Standard and Trial group respectively. Regarding the observation of above parameters in the Control group after treatment, it is suggested that they might have developed some degree of desensitization of Leptin receptors in the hypothalamus, leading to an increase in food intake and blood Leptin levels.

While examining the pathology of *Sthoulya*, it was observed that *Koshtasritha Samana Vayu* became obstructed within the *Medasavritha srothas*, resulting in *Athi santhukshana* of *Jataragni*. The action of Leptin can be understood within the framework of *Prana* and *Samana Vayu. Guduchi Triphala Kwatha* with *Shilajathu* appears to have been effective removing *Srothoavarodha* that obstructed *Samana* and *Prana Vayu* by its *Chedana Karma.*

Additionally, the *Laghu Ruksha Guna* and *Tridoshahara* properties of the *Kwatha* might contribute to this effect. Consequently, the regulation of Leptin levels and food intake, might have been corrected.

Effect on bodyweight, BMI, WC and Adipose tissue: Consumption of HFD increases body weight and visceral fat in the body. This may be viewed under *Medovridhi* in *Sthoulya*. This excess *Medas* have *Snigdha, Sthira, Guru, Pichila* and *Mrdu guna* and are predominant of *Prithvi Jala Mahabhuta.* This may lead to enlargement of *Udara*. The increased adipocyte and fat accumulation might be considered as *Badha Medas* and the increased circulatory free fatty acids as *Abadha Medas*. The ingredients in the *Kwatha* have *Laghu, Ruksha guna* which is opposite to the quality of *Dushta Medas* but not *Vatavardhaka*. Shilajathu possesses *Chedana Karma* which might have helped in removing *Srothorodha* and made the *Kwatha* act effectively on *Medovridhi*.

Effect on Total cholesterol: The circulating lipoproteins might be viewed as *Abadha Medas* having *Pichila, Guru, Snigdha guna*. The ingredients in *Kwatha* by its *Laghu Ruksha Guna* may counteract the properties of *Abadha Medas* and help in reducing them. The *Lekhana, Chedana Karma* of *Prakshepa churna* might also reduce *Abadha Medas.* The increase in HDL levels in trial groups might be due to the *Rasayana guna* of drugs helping in proper formation and excretion of lipoproteins.

Effect on Insulin levels: In the present study, we have the stage of Hyperinsulinemia or the *Agnidushti.* Impaired glucose uptake in cells like muscles and increased circulating free fatty acid may have resulted in insulin resistance leading to increased glucose and insulin levels in blood. This might have been a major pathology of *Mamsa Medo dhtavagni dushti.* Elevated levels of Insulin levels might be viewed under the *Samprapthi* of *Prameha Purvarupa* due to *Sthoulya.* Here insulin resistance might be due to *Medodhtvagnimandhya* which resulted in increased production of insulin. This *Agnidushti* may lead to accumulation of *Vikritha Kleda* in *Rakthavahasrothas* finally resulting in Hyperglycemia. *Guduchi Triphala Kwatha* might be acting on *Mamsa Medo dhathu dushti* as *Shilajathu* is a known drug for *Vasthiroga* or *Prameha* which mainly occurs due to *Mamsa Medo dushti.* This might be the reason for its more pronounced effect in insulin levels.

Effect on Antioxidant Status: MDA, the product of lipid peroxidation, is an important marker for the level of oxygen free radicals. Excessive accumulation of free radicals within

the cells are the end result of improper metabolism. This might be viewed under the mechanism of formation of *Ama* at the *Dhathu level*, as *Ama* is the end product of *Alpagni*. Increased free radicals may impair the activities of antioxidant enzymes and the structure of lipids producing lipid peroxidation and oxidative stress within the cells. This might be understood under *Medodhatvagnimandhya* resulting in *Medodhathu Vridh*i. The *Dipana property* of *Kwatha* might have helped in correcting *Agnidushti* and activities of antioxidant enzymes. All drugs in *Kwatha* and *Prakshepa Churna* having *Rasayana* properties might have helped in reducing *Ama* at the cellular level. Thereby reducing lipid peroxidation and oxidative stress.

Histopathological analysis of Liver and Kidney: The histopathological examination of liver and Kidney in Trial drug showed mild changes when compared to the Control group. Hence the result suggested a safer profile of Trial drug. The minimal changes observed in some parameters may be attributed to the persistent HFD feeding.

CONCLUSION

The combination of *Guduchi Triphala Kwatha* with *Shilajatu* showed significant effect in the obesity parameters. *Shilajatu* is a well-known drug used in treating *Vasti Roga* and it is recognized that insulin resistance is closely linked to the development of Diabetes. Therefore, it might be possible that this combination primarily targets the *Mamsa Medo Dhathu* by reducing the *Dhathvagnimandhya* at the respective level. This action may contribute to relieving obesity by primarily acting on the *Abadha Medas* through correcting insulin levels.

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